

Attorney Docket No.: UMD-0112  
Inventors: Alland and Hazbón  
Serial No.: 10/540,460  
Filing Date: January 17, 2006  
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#### **REMARKS**

Claims 1-11 are pending in the instant application. Claims 8-11 have been withdrawn from consideration by the Examiner and subsequently canceled without prejudice by Applicants herein. Claims 1-7 have been rejected. Claims 1, 2 and 4 have been amended. Support for these amendments is provided in the specification at page 7, line 34 through page 8, line 4, Example 3 beginning at page 15, Example 7 beginning at page 18 and in Figure 1. No new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### **I. Finality of Restriction Requirement**

The Examiner has made final the Restriction Requirement mailed October 17, 2007. Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have canceled without prejudice nonelected claims 8-11. Applicants reserve the right to file a divisional application to the canceled subject matter.

#### **II. Amendment to Specification**

The specification has been amended to include specific reference to the prior-filed applications in compliance with 37 C.F.R. 1.78(a) and as set forth in the Declaration filed in the

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instant application and as recognized by the USPTO on the first filing receipt. No new matter is added by this amendment and entry is respectfully requested.

**III. Rejection of Claims 1-7 under 35 U.S.C. 112, second paragraph**

Claims 1-7 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite and failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Examiner suggests that recitation of the phrase "lower amplification efficiency", "delayed threshold cycle" and "a difference in the amount" is indefinite because these phrases are relative terminology and the claims do not set forth what the phrases are being compared to or with.

In addition, claims 2-4 are suggested to be indefinite over recitation of the phrase "the nucleic acid sequence" because this phrase lacks proper antecedent basis. Claim 4 is also suggested to be indefinite over the recitation of "the PCR reaction" as lacking antecedent basis.

Accordingly, in an earnest effort to advance the prosecution, the claims have been amended to clarify that a lower amplification efficiency or delayed threshold cycle or a

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difference in the amount of amplified product is determined by comparison to amplification efficiency or threshold cycle or amount of amplified product in a reaction containing primer-template matches. Support for this amendment is provided in the specification at page 7, line 34 through page 8, line 4, Example 3 beginning at page 15, Example 7 beginning at page 18 and in Figure 1. Accordingly, no new matter is added by this amendment.

Further, Applicants have amended claims 2 and 4 to correct for antecedent basis.

Withdrawal of this rejection is therefore respectfully requested.

#### **IV. Rejection of Claims 1, 2, 4 and 5 under 35 U.S.C. 102(b)**

Claims 1, 2, 4 and 5 have been rejected under 35 U.S.C. 102(b) as being anticipated by Nazarenko et al. (U.S. Patent No. 6,090,552) as evidenced by GenBank Accession No. NM\_000025. The Examiner suggests that Nazarenko teaches a method for detecting the presence of a single polynucleotide polymorphism or a mutation in a target nucleic acid in an organism wherein the method comprises: (i) amplifying a nucleic acid sequence using a hairpin primer, wherein the hairpin primer terminates at a polymorphic position, such that the 3' nucleotide of the hairpin primer is located at the position of the single nucleotide

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polymorphism or mutation; and (ii) measuring the amount of amplification product wherein a decrease in the amplification product is indicative of the presence of a polymorphism or mutation. The Examiner suggests that Nazarenko teaches that in the method of allele-specific PCR, "(u)nder the appropriate reaction conditions, the target DNA is not amplified if there is a base mismatch." Regarding the recitation in the claims that the method is one which amplifies a 30 to 90 base pair nucleic acid molecule of an organism, the Examiner suggests that the method exemplified by Nazarenko results in amplification of 101 base pairs of the B3AR nucleic acid. Thus, the Examiner suggests that the method of Nazarenko is one in which 30 to 90 bp of a nucleic acid molecule of an organism is amplified since amplification of a 101 base pair region necessarily includes the amplification of 30 to 90 base pairs.

Applicants respectfully traverse this rejection.

At the outset, Applicants respectfully point out that the claims have been amended to recite an assay for detecting a single nucleotide polymorphism in an organism comprising amplifying a short amplicon consisting of 30 to 90 base pairs of a nucleic acid molecule of an organism using a hairpin shaped primer that discriminates between different alleles by situating

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its 3' nucleotide at the location of a single nucleotide polymorphism. Support for this amendment is provided in the specification at page 8, lines 4-10 and page 15, lines 22-26.

Amplification of a short amplicon consisting of 30 to 90 base pairs in the assay of the present invention is clearly different to teachings of Nazarenko et al. acknowledged by the Examiner to teach amplification of 101 base pairs of the B3AR nucleic acid.

MPEP 2131 is clear; to anticipate a claim the reference must teach all the elements of the claims. Since Nazarenko et al. do not teach amplification of a short amplicon consisting of 30 to 90 base pairs, this reference cannot anticipate the instant claimed invention.

Withdrawal of this rejection is therefore respectfully requested.

**V. Rejection of Claims 3 and 6 under 35 U.S.C. 103(a)**

Claims 3 and 6 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al.

With respect to claim 3, the Examiner suggests Nazarenko et al. exemplify methods wherein the hairpin primer comprises DNA, but does not exemplify methods wherein the hairpin primer

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comprises RNA. However, the Examiner suggests that Nazarenko et al. do teach that the hairpin primer may be DNA or RNA.

With respect to claim 6, the Examiner suggests that Nazarenko et al. exemplify methods using allele-specific hairpin primers wherein the PCR amplification products are detected at the completion of the PCR assay, but do not exemplify methods using allele-specific PCR. The Examiner suggests, however, that Nazarenko et al. do teach that in methods in which the amplification product is formed using a hairpin primer, the amplification product can be detected by real-time PCR which is stated to provide advantages of allowing researchers to perform the method in closed tubes, thereby eliminating the risk of carry-over contamination, etc. Thus, the Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Nazarenko et al. so as to have detected the amplification products using real-time PCR in order to have provided an effective means for monitoring the allele-specific amplification reaction which would simplify the detection method, reduce cross-contamination and allow for a highly accurate quantification of the amplification products.

Applicants respectfully traverse these rejections.

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MPEP 2143.03 states "[i]f an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious.

Claim 1, from which claims 3 and 6 depend, is nonobvious from teachings of Nazarenko et al.

In accordance with 35 U.S.C. 103(a), "a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art is such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

As discussed in detail in Section III, supra, Nazarenko et al. do not identically disclose the instant claimed invention. In particular, no where does this reference teach or suggest amplification of a short amplicon consisting of 30 to 90 base pairs. Instead, Nazarenko et al. teach an amplicon of 101 bases.

Further, it would not have been obvious to a person of ordinary skill in the art to modify the amplicon size to a shorter amplicon of 30 to 90 bases, as the typical amplicon size

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is approximately 100 to 300 bases pairs (see teachings in the specification at page 8, lines 4-6).

Thus, the instant claimed invention is not obvious over teachings of Nazarenko et al.

Withdrawal of this rejection is respectfully requested.

#### **VI. Rejection of Claim 7 under 35 U.S.C. 103(a)**

Claim 7 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. in view of Tyagi (U.S. Patent 6,365,729). The Examiner suggests that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Nazarenko et al. so as to have performed the allele-specific PCR method using hairpin primers that contain PNAs in view of the well known benefits provided by PNAs of enhancing the stability of hybridization and improving the ability to distinguish between perfectly matched and mismatched sequences. The Examiner suggests that one would have been motivated to have used PNA hairpin primers in order to have provided a highly sensitive and effective method for detecting the presence of a polymorphism or mutation.

Applicants respectfully traverse this rejection.



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MPEP 2143.03 states "[i]f an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious.

Claim 1, from which claim 7 depends, is nonobvious from teachings of Nazarenko et al. in combination with Tyagi et al.

In accordance with 35 U.S.C. 103(a), "a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art is such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

The cited combination of Nazarenko et al. and Tyagi does not identically disclose the instant claimed invention. In particular, no where does either reference teach or suggest amplification of a short amplicon consisting of 30 to 90 base pairs.

Further, it would not have been obvious to a person of ordinary skill in the art to modify the amplicon size to a shorter amplicon of 30 to 90 bases, as the typical amplicon size

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is approximately 100 to 300 bases pairs (see teachings in the specification at page 8, lines 4-6).

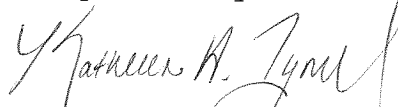
Thus, the instant claimed invention is not obvious over teachings of Nazarenko et al. in view of Tyagi.

Withdrawal of this rejection is respectfully requested.

#### **VII. Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



Kathleen A. Tyrrell  
Registration No. 38,350

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Licata & Tyrrell P.C.  
66 E. Main Street  
Marlton, New Jersey 08053

(856) 810-1515